

REMARKS

This paper is responsive to the Advisory Action dated December 22, 2008 and further supplements Applicants' response filed on December 12, 2008. Applicants gratefully acknowledge that the Examiner has entered the claim amendments filed on December 12, 2008 in response to the final Office Action dated June 12, 2008. Applicants also respectfully submit that this paper only clarifies certain issues previously considered by the Examiner and does not raise any new issues nor amends any of the pending claims.

In the Advisory Action, the Examiner has indicated that pending claims 58 to 60 and 62 to 83 are rejected and none of the pending claims are allowed. Applicants have set forth the complete set of pending claims in this response and have not made any further claim amendments.

Applicants respectfully note that claims 77 and 78 were allowed in the final Office Action dated June 12, 2008. Since the Advisory Action has not cited any new references or set forth specific arguments against claims 77 and 78, Applicants respectfully request that the rejections of claims 77 and 78 be withdrawn and the allowance thereof be restated.

With respect to the definition of "zwitterionic compound", the Examiner has asserted that the IUPAC definition of the term does not appear to exclude the zwitterionic compounds having charges on adjacent atoms. Thus, the Examiner has disagreed with Applicants' arguments that none of the Haugland (US 6,972,326) dyes contain a zwitterionic dye moiety.

It is true that Applicants have cited the IUPAC definition for "zwitterionic compound" in the response dated December 12, 2008, but Applicants have not argued that the Haugland dyes do not contain a zwitterionic dye moiety because the Haugland dyes have charges on adjacent atoms. In the response dated December 12, 2008, Applicants stated: "...Zwitterionic compounds have no uncharged canonical representations. For example: $\text{H}_3\text{N}^+\text{CH}_2\text{C}(=\text{O})\text{O}^-$; glycine... Thus, the BODIPY dyes of Haugland are not zwitterionic compounds." That is, the BODIPY dyes of Haugland are not zwitterionic compounds because the BODIPY dyes have uncharged canonical representations. More specifically, as shown below, although the BODIPY dyes can be represented by a chemical structure having both positive and negative charges, they can also be represented by an uncharged chemical

structure. In other words, BODIPY dyes have uncharged canonical representations and thereby are not zwitterionic compounds.



BODIPY Core

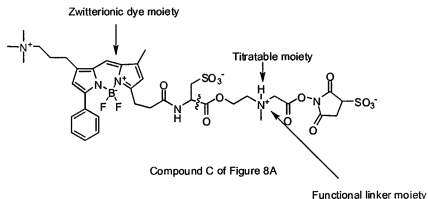


BODIPY Core

For example, the Glossary of Terms Used in Physical Organic Chemistry recommended by IUPAC (a copy enclosed for purposes of clarification) defines the term “zwitterionic compound” as “a neutral compound having electrical charges of opposite sign, delocalized or not on adjacent or nonadjacent atoms. Zwitterionic compounds have no uncharged canonical representations. Sometimes referred to as inner salts, ampholytes, dipolar ions (a misnomer).” (underline added) Another Chemistry Dictionary widely used by chemists, namely, the Chemistry Dictionary of ChemiCool.com (a copy enclosed), also states that zwitterionic compounds have no uncharged canonical representations. It is important to note that Haugland shows the uncharged canonical representations of the BODIPY dyes throughout the disclosure. Therefore, since the BODIPY dyes have uncharged canonical representation, they are not zwitterionic compounds. Furthermore, Applicants respectfully note that the enclosed definitions for “zwitterionic compound” are commonly known to a chemist skilled in the art and are provided for the purpose of further clarifying Applicants’ remarks submitted on December 12, 2008. Thus, the enclosed definitions do not raise any new issues.

The Examiner has also alleged that Applicants cited a zwitterionic dye moiety whereby the charges are on adjacent atoms in Applicants’ response filed on July 11, 2007. To clarify this issue, Applicants have reproduced the chemical structure in the response dated July 11, 2007 below. As shown by the chemical structure, Compound C of Figure 8A has a “zwitterionic dye moiety” and a “functional linker moiety” which are divided by a short waved line. That is, the “zwitterionic dye moiety” includes the piece of Compound C covering the quaternary amine having a positive charge as well as the sulfonate group having a negative charge. The BODIPY moiety is only a portion of the “zwitterionic dye moiety”. Applicants respectfully submit that the dye moiety shown below is zwitterionic because it contains the quaternary amine having a positive charge and the sulfonate group having a negative charge, not because it contains a BODIPY moiety. Furthermore, the quaternary amine and the sulfonate group have no uncharged canonical representation between pH 3 and

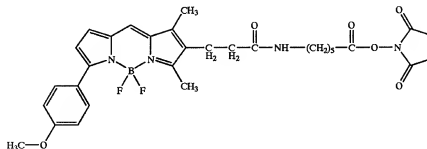
11. Thus, Applicants' recitation of Compound C as a zwitterionic compound is consistent with both the widely accepted definition for "zwitterionic compound" and Applicants' remarks regarding the same.



Chemical Structure in the Response Dated July 11, 2007

To rebut Applicants' arguments regarding the titratable group moiety, the Examiner has asserted that Haugland (US 6,972,326) discloses a tertiary amine in the compound of claim 18.

Applicants respectfully disagree with the Examiner and submit that claim 18 of Haugland does not disclose a tertiary amine. As shown below, the compound of claim 18 of Haugland contains two nitrogen atoms that are not in the dye moiety. One of the nitrogen atoms, taken together with the adjacent carbonyl, forms an amide group; while the other nitrogen atom, taken together with the adjacent two carbonyl and one oxygen, forms a hydroxysuccinimide group. Inasmuch as the amide group is not considered as a secondary amine by a chemist of ordinary skill, the hydroxysuccinimide group is a separately recognized functional group which is not considered as a tertiary amine.



Compound of Claim 18 of Haugland

Furthermore, Applicants respectfully note that the titratable group moiety, as claimed in the present invention, not only is a tertiary amine, but also closely approximates the pK of the group removed from the analyte by reaction with the functional linker. As discussed in detail in the Response filed December 12, 2008, even if, *arguendo*, Benson discloses tertiary amines, the Benson tertiary amines do not approximate the pK of the group removed from the analyte by reaction with the functional linker. Thus, Applicants respectfully submit that none of the cited references disclose a titratable group moiety which is a tertiary amine closely approximating the pK of the group removed from the analyte by reaction with the functional linker, as claimed in the present invention.

In view of the foregoing explanation and the remarks in the Response filed on December 12, 2008, Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness because the cited references, when combined, fail to teach or suggest all the claim limitations of the present invention.

Conclusion

For the reasons stated above, Applicants respectfully request reconsideration of the arguments made in the response filed on December 12, 2008 and in the further arguments and explanations with supporting dictionary definitions provided herewith. As discussed above, the present supplemental response does not raise any new issues. Applicants submit that the claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicant respectfully requests a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite the eventual allowance of the claims.

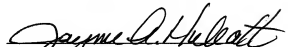
Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. 1.136(a)(3).

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